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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/914,020	12/31/2001	Yuehua Li	5051-451IP	8515

20792 7590 08/28/2006

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EXAMINER	
EPPS FORD, JANET L	
ART UNIT	**PAPER NUMBER**
1633	

DATE MAILED: 08/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/914,020	LI ET AL.	
	Examiner	Art Unit	
	Janet L. Epps-Ford	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *78-80,82,85-89,91-93,95-97 and 99-115* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *78-80,82,85-89,91-93,95-97 and 99-115* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 78-80, 82, 85-89, 91-93, 95-97, 99-109, and 111-115 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. (Written Description/New Matter), for the reasons of record, and for those set forth below.

4. Applicants traversed the instant rejection on the grounds that the present amendment more clearly defines the invention:

> In response to this rejection, applicants have amended the claims to more clearly define their invention. Independent amended claims 78, 85 and 91 clearly define that the myristoylated peptide fragment consists of from about 10 to about 50 contiguous amino acids from the N-terminal glycine residue of the MARCKS protein as shown in SEQ ID NO: 4 and further recites that the peptide inhibits MARCKS protein-related mucus hypersecretion. This language defines that the claimed peptides begin at the N-terminal glycine and range from about 10 contiguous amino acids up to about 50 contiguous amino acids of MARCKS protein as defined by SEQ ID NO:4. All of the dependent claims from these three independent claims contain this same feature.

5. The instant claims have been amended to recite: "a myristoylated peptide fragment of the N-terminal region of the MARCKS protein consisting of ***from about*** 10

to ***about*** 50 contiguous amino acids beginning from the N-terminal glycine residue of the MARCKS protein as shown in SEQ ID NO: 4." The scope of this phrase encompasses the following interpretations: a) wherein the myristoylated peptide fragment consists of from about 10 to about 50 contiguous amino acids from the N-terminal region of the MARCKS protein, wherein said N-terminal region of the MARCKS protein begins from the N-terminal glycine residue of SEQ ID NO: 4; b) wherein the myristoylated peptide fragment, consists of a fragment of the N-terminal region of the MARCKS protein, wherein said N-terminal region of the MARCKS protein consists of ***from about*** 10 to ***about*** 50 continuous amino acids beginning from the N-terminal glycine residue of SEQ ID NO: 4.

6. Due to the ambiguity associated with the phrase "from about" as recited in the instant claims, and the various interpretations possible regarding the scope of the instant claims, the extent of the N-terminal region of the MARCKS protein remains ambiguous. Therefore the structures of the myristoylated peptide fragments of the N-terminal region of MARCKS that function to inhibit mucous secretion remain ambiguous, for the reasons of record.

Based upon the Parikh Declaration previously submitted by Applicants, it is clear that the first 10 amino acids of the MARCKS protein are essential to mucus inhibition. However, there is no evidence that other fragments of the N-terminal region of the MARCKS protein that do not contain this minimal sequence would function in mucus inhibition. As stated above, due to the ambiguity associated with the present amendment, it is unclear if the phrase "from about 10 to about 50 contiguous amino

acids" set forth in the instant claims refers to the structure of the peptide fragment of the N-terminal region, ***or*** if the phrase provides a definition of the structure of the N-terminal region of the MARCKS protein, such that the scope of the peptide fragments can include fragments other than those including the first 10 amino acids beginning from the N-terminal glycine residue of SEQ ID NO: 4.

Moreover, in regards to claims 95-97, 99, 101-105, and 107-109, which recite the phrase "MANS peptide," the specification as filed provides only support for wherein the MANS peptide is myristic acid-SEQ ID NO: 1, there is no other sequence given in the specification as filed that defines the MANS peptide. However, since the instant claims are not limited to any particular sequence structure it is unclear what other sequence structures are encompassed by the term "MANS peptide" as recited in the claims. For example, it is unclear if the term encompasses variants of undefined length and origin corresponding to the MANS peptide.

Additionally, the range of "from about 10 to about 20," recited in instant claims 113-115, does not find support in the specification or claims as originally filed. The original claims provide support for the range "from about 10 to about 50," and the specification as filed provides support for peptides of 24 and 25 amino acids in length. However, there is no support for the range recited in these claims. Applicants are requested to remove the new matter in response to this Office Action.

7. Claims 78-80, 82, 85-89, 95-97, 99-106, and 111-114 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for inhibiting mucus secretion *in vitro,* and for decreasing mucus hypersecretion in vivo via airway

administration of the MANS-peptide or active fragments thereof comprising at least the first 10 amino acids of the MANS-peptide in a mouse model of asthma, does not reasonably provide enablement for the *in vivo* therapeutic treatment of bronchitis, cystic fibrosis, chronic obstructive pulmonary disease comprising administration of the compounds of the instant invention. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims, for the reasons of record.

8. In regards to the Rogers Declaration under 1.132, and Applicant's arguments filed 6-07-2006, it is noted that both Applicant and the Declaration relies heavily upon data submitted in post-filing references to support the assertion of full enablement of the instantly claimed invention. The instant specification has a priority date of 2/24/2000, yet references are provided that were published in 2004 (Exhibit 5), Li et al. 2001 (Exhibit 6), Singer 2004 (exhibit 7), and Rogers (Exhibit 8). Furthermore, it is unclear that the experimental data produced in the cited references were produced using the guidance that is set forth in the specification as filed. See MPEP § 2164.05 that states "[T]o overcome a prima facie case of lack of enablement, applicant must demonstrate by argument and/or evidence that *the disclosure, as filed*, would have enabled the claimed invention for one skilled in the art *at the time of filing.*" The specification as filed provides only *in vitro* data. The Parikh Declaration provided post-filing *in vivo* data using the MANS peptide and active fragments of the MANS peptide to produce inhibition of mucin hypersecretion in the mouse model of asthma. However there is no evidence that the mouse model of asthma used in the Parikh Declaration would be

predictive of the efficacy of the MANS peptide or fragments for the treatment of full scope of diseases encompassed by the instant claims.

While the specification relies upon inhibiting mucin secretion with SEQ ID NO: 1 as an assay for MANS peptide activity (see paragraph 71 of the instant specification), there is no correlation between merely inhibiting mucous secretion and the *in vivo* production of therapeutic effects in patients suffering from diseases or conditions such as bronchitis, asthma, cystic fibrosis, chronic obstructive pulmonary disease, bronchiectasis, emphysema, pneumonia, influenza, rhinitis, and the common cold. There is no evidence of record that demonstrates that the MANS peptide would function to modulate all inflammatory mediators associated with the full scope of diseases encompassed by the instant claims. The lack of any working *in vivo* examples in the specification as filed is exacerbated because the invention is in a highly unpredictable art-regulating the airway mucus hypersecretion-and while the level of skill of a practitioner in the art may be high, the state of the art at the time of the instant invention was in fact unknown and untested in regards to the administration of peptide fragments for the treatment of disorders such as bronchitis, cystic fibrosis, COPD, etc.

Double Patenting

9. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Omum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double

patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

10. Claims 78-80, 82, 85-89, 91-93, 95-97, and 99-115 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 52-54, 57-67, 70-75 and 85-91 of copending Application No. **10/802,644**. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are expressly claiming the same subject mater, although they differ in scope. The instant claims and those of the copending application are drawn to the same methods of regulating the same mucus secretion in the airways of patient populations with the same compositions to achieve the same therapeutic effect of the instant application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Epps-Ford whose telephone number is 571-272-0757. The examiner can normally be reached on M-F, 9:30 AM through 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave T. Nguyen can be reached on 517-272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Janet L. Epps-Ford
Primary Examiner
Art Unit 1633

JLE

DAVE TRONG NGUYEN
SUPERVISORY PATENT EXAMINER